

Amendment to the Drawings:

Please amend the drawings as follows:

The attached replacement sheets are replacement sheets for Figures 26a, 26b, 26c and 26d. No changes have been made; however, the replacement sheets are clearer than the sheets as filed.

Attachment: Replacement sheet (one sheet)

REMARKS

Interview request

Applicants respectfully request a telephonic interview after the Examiner has reviewed the instant response and amendment. Applicants request the Examiner call Applicants' representative at (858) 720-5133.

Status of the Claims

Pending claims

Claims 1 to 36, 39 and 40 are pending. Claims 14, 18, 19 and 22, are withdrawn from consideration.

Claims added and canceled

Claims 41 to 47 are added, and claims 17 to 20 are canceled, without prejudice or disclaimer. Thus, after entry of the instant amendment, claims 1 to 16, 21 to 36, 39 and 40 to 47, will be pending and under consideration.

Summary outstanding objections, rejections and traversal

Claims 8, 10, 12, 23 and 30 are objected to.

Claims 1 to 13, 15 to 17, 20, 21, 23 to 36, 39 and 40 are rejected under 35 U.S.C. §112, second paragraph.

Claims 1, 5, 6, 8 to 10, 21, 35, 36, 39 and 40 are rejected under 35 U.S.C. §102(e), over Peterson, et al., U.S. Patent No. 5,783,431.

Claims 1 to 6, 8 to 13, 15, 16, 24 to 28, 30, 31, 34, 39 and 40, are rejected under 35 U.S.C. §103(a), over Perlman, et al., U.S. Patent No. 4,801,529, in view of Peterson.

Claim 7 is rejected under 35 U.S.C. §103(a), over Perlman in view of Peterson in further view of McCabe, U.S. Patent No. 5,593,829.

Claim 20 is rejected under 35 U.S.C. §103(a), over Perlman in view of Peterson in further view of Knazek, U.S. Patent No. 3,883,393.

Claim 20 is rejected under 35 U.S.C. §103(a), over Perlman in view of Peterson in further view of Saxena, U.S. Patent No. 4,833,083.

Claim 20 is rejected under 35 U.S.C. § 103(a), over Perlman in view of Peterson in further view of Weaver, U.S. Patent No. 4,959,301.

Applicants respectfully traverse the objections to the specification and rejections to the claims.

Support for the claim amendments

The specification sets forth an extensive description of the invention in the amended claims. Other support can be found in the claims as originally filed. For example, support for a column comprising an inlet and an outlet for the flow of a liquid, e.g., a culture media, can be found, *inter alia*, in the paragraph spanning pages 168 to 169 of the specification (see paragraph [0698] of the '005 publication), and Figure 24; wherein the system comprises a pumping mechanism for moving media from one end of the column (the inlet) to another end (the outlet), can be found, *inter alia*, in the first full paragraph of page 169 (see paragraph [0699] of the '005 publication), and Figure 24. Support for a claim encompassing use of various culture media can be found, *inter alia*, in paragraph [0683] of the '005 publication. Support for a claim encompassing culturing encapsidated cells for varying periods of time can be found, *inter alia*, in paragraphs [0701], [0139] and [0683], of the '005 publication. Support for a claim encompassing culturing various specific types of cells can be found, *inter alia*, in paragraphs [0685] and [0686], of the '005 publication. Claim 20 is rejected under 35 U.S.C. § 103(a), over Perlman in view of Peterson in further view of Saxena, U.S. Patent No. 4,833,083.

Accordingly, no new matter has been added by way of these amendments.

Drawings

The Office requested new Figures 26a to 26d; see paragraph 2, page 2, of the OA. The instant amendment to the drawings – providing replacement sheets – addresses this issue. Kindly substitute the enclosed drawings for the previously submitted drawings.

No changes have been made in the replacement sheets – however, the replacement sheets are clearer than the drawings as filed; specifically, the size of the numbers, letters, and reference characters has been corrected with regard to Figure 26A-D, so as to be in accordance with 37 CFR 1.84 (p). Favorable consideration of the enclosed drawings is respectfully requested.

Specification

The Office requested the priority information in the first paragraph of the specification be updated; see page 2, paragraph 3, of the OA. The instant amendment to the specification addresses this issue, and also corrects an inadvertent error in the serial number of one of the priority documents. A supplemental Application Data Sheet (ADS) and a corrected and inventor-executed Rule 63 declaration further addressing this issue is submitted herein.

Claim Objection

Claims 8, 10, 12, 23 and 30 are objected to, as discussed in detail in paragraphs 4 to 7, pages 2 to 3, of the OA. The instant amendment addresses this issue.

Issues under 35 U.S.C. §112, second paragraph

Claims 1 to 13, 15 to 17, 20, 21, 23 to 36, 39 and 40 are rejected under 35 U.S.C. §112, second paragraph, for reasons set forth in detail on pages 3 to 4, paragraphs 8 to 14, of the OA. The instant amendment addresses this issue.

Issues under 35 U.S.C. §102(e)

Claims 1, 5, 6, 8 to 10, 21, 35, 36, 39 and 40 are rejected under 35 U.S.C. §102(e), over Peterson, et al., U.S. Patent No. 5,783,431, filed October 24, 1996, issued July 21, 1998 (hereinafter "Peterson"), for reasons set forth in detail on pages 4 to 5, paragraphs 15 and 16, of the OA. The instant amendment addresses this issue.

The legal standard for anticipation under 35 U.S.C. §102 is one of strict identity. To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention. In re Paulson, 30 F.3d 1475, 1478-79, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994) (citing In re Spada, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990)). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). MPEP §2131; pg 2100-67, 8th ed., Rev. 5, August 2006.

The instant amendment clarifies that the (amended) claimed methods of the invention encompass use of, *inter alia*, a system for isolating, maintaining and/or culturing cells in porous microdroplets, where the system comprises a growth column with an inlet and an outlet, and a mechanism for moving or circulating a growth medium through the length of the growth column, wherein the growth column comprises openings at either end of the column to allow the culture media to flow through the length of the column. In this claimed embodiment, a mixed population of uncultivated cells is encapsulated into a porous microdroplet; then, the cell-comprising porous microdroplets are “cultured” in the growth column with the “flowing” culture media.

In contrast, Peterson only described use of sterile flasks – see, e.g., lines 1 to 2, column 43, of Peterson – (as noted by the Office in lines 1 to 2, page 5, of the OA) and multi-well plates – see, e.g., lines 14 to 21, column 44, of Peterson (“subsequent culturing may be done in multi-well plates”).

Thus, Peterson is defective in that it does not teach or suggest use of, *inter alia*, a system for isolating, maintaining and/or culturing cells in porous microdroplets, where the system comprises a growth column with an inlet and an outlet, and a mechanism for moving or circulating a growth medium through the length of the growth column, wherein the growth column comprises openings at either end of the column to allow the culture media to flow through the length of the column. Accordingly, because Peterson is not a single prior source that contains each and every limitation of the claimed invention, the rejection under section 102(e) can be properly withdrawn.

Issues under 35 U.S.C. §103(a)

Perlman in view of Peterson

Claims 1 to 6, 8 to 13, 15, 16, 24 to 28, 30, 31, 34, 39 and 40 are rejected under 35 U.S.C. §103(a), over Perlman, et al., U.S. Patent No. 4,801,529, filed January 31, 1989, issued January 31, 1989 (hereinafter “Perlman”), in view of Peterson, for reasons set forth in detail on pages 6 to 10, paragraphs 17 and 18; and, paragraphs 23 and 24, pages 15 and 16, of the OA. The instant amendment addresses this issue.

The Office cited Perlman for teaching *inter alia* various cells in various microenvironments, as discussed in detail, e.g., from line 4, page 7, to line 7, page 9, of the OA. The Office notes that

Perlman does not teach placing and incubating an encapsulated cell in a growth column, see e.g., lines 8 to 9, page 9, of the OA, and defines how the term “column” was interpreted for purposes of this examination in line 10 to 12, page 9 (see also the sentence spanning pages 4 to 5, of the OA).

Because Peterson is defective in that it does not teach or suggest use of, *inter alia*, a system for isolating, maintaining and/or culturing cells in porous microdroplets, where the system comprises a growth column with an inlet and an outlet, and a mechanism for moving or circulating a growth medium through the length of the growth column, wherein the growth column comprises openings at either end of the column to allow the culture media to flow through the length of the column, and because Perlman does not teach any growth column, Peterson cannot be used to correct the defects in Perlman to teach the (amended) claimed methods (neither Peterson nor Perlman in any combination teach or suggest the (amended) claimed methods). Accordingly, the section 103 rejection based on Perlman in view of Peterson can be properly withdrawn.

Perlman in view of Peterson, and in further view of McCabe

Claim 7 is rejected under 35 U.S.C. §103(a), over Perlman in view of Peterson in further view of McCabe, U.S. Patent No. 5,593,829, filed May 3, 1994, issued January 14, 1997 (hereinafter “McCabe”), for reasons set forth in detail on pages 10 to 12, paragraph 19, of the OA. The instant amendment addresses this issue.

The Office notes that neither Perlman nor Peterson teach use of various biological samples, see e.g., page 11, lines 2 to 5, of the OA; and cited McCabe for teaching these specific samples (see e.g., page 11, lines 6 to 7, of the OA).

However, as discussed above, in light of the instant claim amendment: because Peterson is defective in that it does not teach or suggest use of, *inter alia*, a system for isolating, maintaining and/or culturing cells in porous microdroplets, where the system comprises a growth column with an inlet and an outlet, and a mechanism for moving or circulating a growth medium through the length of the growth column, wherein the growth column comprises openings at either end of the column to allow the culture media to flow through the length of the column, and Perlman does not teach any growth column – and because McCabe also does not teach any growth column, McCabe cannot be used to cure this defect in Perlman and Peterson. Accordingly, the section 103 rejection based on Perlman in view of Peterson in further view of McCabe can be properly withdrawn.

Perlman in view of Peterson, and in further view of Knazek

Claim 20 is rejected under 35 U.S.C. §103(a), over Perlman in view of Peterson in further view of Knazek, U.S. Patent No. 3,883,393, filed February 11, 1974, issued May 13, 1975 (hereinafter “Knazek”), for reasons set forth in detail on pages 12 to 13, paragraph 20, of the OA. The instant amendment addresses this issue; claims 17 to 19 are canceled.

Knazek was cited for teaching culturing cells in a growth column (see, e.g., lines 7 to 8, of paragraph 20, page 12, of the OA).

Because the limitation of using growth columns has been incorporated into claim 1 in this amendment, Applicants wish to emphasize that, as noted in Example 18 of the specification (see paragraph [0688] of the ‘005 publication, and page 166, lines 8 to 16, of the specification):

[0688] Thus, the application of this novel high throughput cultivation method resulted in the growth and isolation of several bacteria representing previously uncultured phylotypes (see supplementary information). This reflects the ability of GMDs to permit the simultaneous and non-competitive growth of both slow and fast growing microorganisms in media with very low substrate concentrations. The physical separation of cells (contained in the GMDs within the growth columns), combined with flow cytometry isolation of microcolonies at different times of incubation, enabled the cultivation of a broad range of bacteria, and prevented over-growth by the fast growing microorganisms (the “microbial weeds”). [emphasis added]

Thus, practicing the (amended) claimed method – a novel high throughput cultivation method encompassing use of microencapsulated cells and growth columns – resulted in the growth and isolation of several bacteria representing *previously uncultured* phylotypes.

Perlman in view of Peterson, and in further view of Saxena

Claim 20 is rejected under 35 U.S.C. §103(a), over Perlman in view of Peterson in further view of Saxena, U.S. Patent No. 4,833,083, filed May 26, 1987, issued May 23, 1989 (hereinafter “Saxena”), for reasons set forth in detail on pages 13 to 14, paragraph 21, of the OA. The instant amendment addresses this issue; claim 20 is canceled.

Saxena was cited for teaching how to culture cells in a chromatography column (see, e.g., line 7 to 8, of paragraph 21, page 13, of the OA).

Because the limitation of using growth columns has been incorporated into claim 1 in this amendment, Applicants wish to emphasize that, as noted in Example 18 of the specification (see paragraph [0688] of the ‘005 publication, and page 166, lines 8 to 16, of the specification):

[0688] Thus, the application of this novel high throughput cultivation method resulted in the growth and isolation of several bacteria representing previously uncultured phylotypes (see supplementary information). This reflects the ability of GMDs to permit the simultaneous and non-competitive growth of both slow and fast growing microorganisms in media with very low substrate concentrations. The physical separation of cells (contained in the GMDs within the growth columns), combined with flow cytometry isolation of microcolonies at different times of incubation, enabled the cultivation of a broad range of bacteria, and prevented over-growth by the fast growing microorganisms (the "microbial weeds"). [emphasis added]

Thus, practicing the (amended) claimed method – a novel high throughput cultivation method encompassing use of microencapsulated cells and growth columns – resulted in the growth and isolation of several bacteria representing *previously uncultured* phylotypes.

Perlman in view of Peterson, and in further view of Weaver

Claim 20 is rejected under 35 U.S.C. §103(a), over Perlman in view of Peterson in further view of Weaver, U.S. Patent No. 4,959,301, filed April 22, 1988, issued September 15, 1990 (hereinafter "Weaver"), for reasons set forth in detail on pages 14 to 15, paragraph 22, of the OA. The instant amendment addresses this issue.

Weaver is cited for teaching use of flow cytometry to sort by size microdroplets comprising encapsulated microcolonies (see, e.g., line 7 to 10, of paragraph 22, of page 14).

However, as discussed above, in light of the instant claim amendment: because Peterson is defective in that it does not teach or suggest use of, *inter alia*, a system for isolating, maintaining and/or culturing cells in porous microdroplets, where the system comprises a growth column with an inlet and an outlet, and a mechanism for moving or circulating a growth medium through the length of the growth column, wherein the growth column comprises openings at either end of the column to allow the culture media to flow through the length of the column, and Perlman does not teach any growth column – and because Weaver also does not teach any growth column, Weaver cannot be used to cure this defect in Perlman and Peterson. Accordingly, the section 103 rejection based on Perlman in view of Peterson in further view of Weaver can be properly withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, Applicants respectfully aver that the Examiner can properly withdraw the objections to the claims the rejection of the pending claims under 35 U.S.C. §112, second paragraph, 35 U.S.C. §102(b) and 35 U.S.C. §103(a). In view of the above, claims in this application after entry of the instant amendment are believed to be in condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to issue.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **564462008100**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

As noted above, Applicants have requested a telephone conference with the undersigned representative to expedite prosecution of this application. After the Examiner has reviewed the instant response and amendment, please telephone the undersigned at (858) 720-5133.

Dated: June 6, 2007

Respectfully submitted,

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